Appendix E

CONCENTRATION-RESPONSE RELATIONSHIPS FOR MODEL SENSITIVITY ANALYSIS IN RISK ASSESSMENT

The interpretation of specific concentration-response relationships is understood to be one of the most problematic issues at this time for the assessment of health risks associated with exposure to ambient PM. The approach to addressing this issue taken in the risk assessment discussed in Chapter VI and in the technical support documents (Abt Associates, 1996a,b) is to consider alternative concentration-response models through a sensitivity analysis. The sensitivity analysis is intended to develop ranges of estimated risks, without attempting to develop any single best estimate of health risks. One of the elements needed to frame such a sensitivity analysis is the development of alternative PM concentration ranges over which reported concentration-response functions would be applied. Alternative approaches to identifying appropriate PM concentration cut-points which define the lower end of such ranges are discussed below. The application of these approaches to a number of epidemiological studies using PM_{10} and $PM_{2.5}$ indices of exposure for mortality, hospital admissions, and respiratory effects in children is also presented.

A. Alternative Approaches to Defining Concentration Cutpoints

The characterization and interpretation of observed PM concentration-response relationships are of particular importance in adequately assessing risks from ambient PM. Varying degrees of uncertainty exist concerning the PM concentration-response relationship. Such uncertainties may limit the ability to discriminate between a range of plausible alternative concentration-response relationships, and this in turn weakens the ability to estimate potential risks associated with exposure to PM, especially at low ambient concentrations[1]. Key issues for consideration include: 1) what tests and procedures have been done to examine the possibility of linear versus nonlinear dose-response relationships; 2) to what degree do statistical uncertainty and inadequate power preclude exclusion of different alternative concentration-response

[1] The terminology of "low" or "lower" concentrations is used to simply refer to observed PM concentrations generally within the lower half to twenty-five percentile of the reported observations, rather than any concentrations "lower" than those observed.

functions; and 3) how factors such as measurement error or copollutants may potentially obscure an underlying concentration-response relationship substantially different and possibly less linear than the reported apparently linear relationship.

Epidemiological investigations of PM generally have taken several approaches to addressing the shape of the concentration-response relationship. A number of investigators have addressed possible non-linearity in this relationship by the use of categorical variables (CD, p. 12-18). Using categorical variables (e.g., quintiles, quartiles) disaggregates the PM concentration spectrum into discrete ranges, and allows risk estimates to be generated independently for each interval. This may increase the likelihood for detecting those ranges of PM concentrations that may be associated with little risk from those associated with substantially higher risk. However, by partitioning the PM data into smaller groups, this procedure may increase the impact of measurement error and reduce the statistical power of the analyses. (CD, p.12-18). More recent studies (1993-on) have used various nonparametric approaches--locally estimated smoothing, cubic splines, etc.-- applicable in Generalized Additive Models to allow better assessment of nonlinearities in the PM concentration-response relationships, as well as control for confounders such as weather, season, and time trends (CD, p. 12-19). In addition, potential nonlinearity in these nonparametric concentration-response models are often assessed through statistical tests as well.

In the base case risk analyses described in Chapter VI, reported linear concentration-response functions have been applied across the range of reported PM concentrations, when available, with estimated risk never being quantified below estimate of PM background concentrations. However, given the uncertainty concerning PM concentration-response relationships, especially at lower concentrations, alternatives to the base case assumptions are examined through a sensitivity analysis. Of particular interest is the possibility of substantial nonlinearity -- i.e., a less steep or zero slope in PM concentration-response relationships at lower concentrations. To address such possibilities, concentration-response information from key studies can be assessed to determine for which concentrations it may be most reasonable to posit a reduced or zero slope in the concentration-response relationship.

Several approaches to determine possible cutpoint PM concentrations of particular interest for use in modeling alternative concentration-response relationships are discussed below. Staff recognizes that no consensus exists on the best approach to identify, test, or interpret the effect of such cutpoints on concentration-response information. Detailed evaluation of concentration-response relationships is made more difficult by a lack of information on data densities and confidence intervals (CD, 12-310-311). Given these circumstances, alternative approaches are used to generate a range of potential cutpoints, with no attempt to identify the best or most appropriate cutpoint for risk assessment purposes.

The overall approach taken here is to evaluate the extent to which detailed concentration-response information from key studies suggests statistical limitations or nonlinearities in PM concentration-response relationships over the range of PM concentrations observed in the studies. This evaluation focuses on lower concentrations ranges, given that several concerns raised about PM concentration-response relationships center on whether reported linear functions may be disguising flat or essentially flat relationships (i.e., show no increase in risk) in the lower portions of the concentration-response relationship. Three approaches, identified as "lower limit of detection," "minimum mean concentration," and "visual interpretation" are defined below. These approaches have been used to identify reasonable cutpoint concentrations for the concentration-response model sensitivity analysis.

- Lower Limit of Detection: A number of studies present concentration-response information which suggests a generally monotonic increase in response as PM increases (CD, p. 12-23, 12-309). Even if such studies for which the concentration-response information does not suggest a substantially nonlinear relationships across the range of data, the ability to detect any potential effects thresholds or other nonlinearities is limited by the data (CD, p. 12-309-311). For example, plots of RR as a function of the quantile PM concentrations are inherently not able to detect any nonlinearities that may be present within the lowest quantile (CD, p.12-309-310). Thus, for studies that only present concentration-response information in quantile plots and do not show apparent nonlinearities, the maximum concentration (the 20th or 25th percentile value for quintile

and quartile plots, respectively) of the lowest quantile can be considered to be the lower limit of detection of possible nonlinearities.

Reported concentration-response relationships using nonparametric smoothed curves allow a much better assessment of nonlinearities in the concentration-response model (CD p.12-19). Statistical tests can be performed to indicate whether any fluctuations seen in these smoothed curves reflect a substantially nonlinear overall relationship that is statistically discriminable from a linear relationship . Limited numbers of air quality observations can reduce the power of this test, however, and even the visual presentations of smoothed curves are not able to discriminate nonlinearities in regions where there are not enough data points to obtain a stable curve shape (CD, p. 12-310). For studies in which an overall linear relationship cannot be statistically rejected and substantial nonlinearities are not evident, the lower limit for detection of nonlinearity may be considered to be around the 10th percentile. Use of the 10th percentile reflects the greater sensitivity of these smoothing methods compared to quantile analyses to examine whether an observed linear relationship appears to hold toward the lower end of the range of observed concentrations.

- Minimum Mean Concentration: The second approach considered is to use a central tendency concentration as the cutpoint of interest, which is generally available for all studies. The mean (or median) concentration may serve as a reasonable cutpoint of increased PM health risk since at this point there is generally the greatest confidence (i.e., the smallest confidence intervals) in the association and the reported RR estimates. The mean concentration considered by staff as most informative to test implications of potential alternative concentration-response functions is the minimum mean concentration associated with a study or studies reporting statistically significant increases in risk across a number of study locations, provided that the monitoring data is sufficient and representative of the area to which the RR estimate is applied. Alternatively, averages of mean concentrations across a group of locations or studies may be more appropriate if location-specific data are inadequate.

- Visual Interpretation: Concentration-response relationships reported by some studies sometimes visually suggest that nonlinearities may exist within the range of the data, even when PM concentrations are significantly associated with health effects in a linear model. Caution is warranted in any visual interpretation of available PM concentration-response information, given the limited information provided and the amount of measurement error that often is involved (CD, p.12-309-311). Use of quantiles can exacerbate this problem as it might increase the likelihood of identifying an apparent nonlinearity in the effect estimate entirely due to increased uncertainty in each quantiles' smaller sample size.

In conjunction with the use of these methods to identify cutpoints for estimating adjusted concentration-response functions, consideration is given to adjustments to the slope of the reported concentration-response relationship. If an underlying nonlinearity is present, the reported slope of a linear concentration-response relationship would change both below the cutpoint concentration (where the reported slope would be too high) and above the cutpoint concentration (where the reported slope would be too low). Adjustments to the slopes of such segments in concentration-response relationships used in this sensitivity analysis are described in the technical support documents (Abt Associates, 1996a,b).

B. Concentration Cutpoints from Key Studies

The three methods described above were applied where appropriate to the studies used in the risk assessment (Table VI-2 in section VI.B of this Staff Paper), including both PM_{10} and $PM_{2.5}$ studies where applicable, for mortality, hospital admissions, and respiratory symptoms effects. As outlined below, judgments are necessary to apply such methods, and staff recognizes that other judgments could reasonably be made. However, staff believes that the approach taken here is reasonable and results in selected cutpoints that are useful for the purpose of defining sensitivity analyses that help to address uncertainties in the quantitative assessment of risks based on the available epidemiological evidence. Following the identification of a number of potential cutpoints from these alternative approaches, summarized in Tables E-1 and E-3, the last section condenses this information into a few selected cutpoints, for use in the sensitivity analyses presented in section VI.C of this Staff Paper.

1. Concentration-Response Relationships Associated with Short-Term PM Exposures

The potential concentration cutpoints identified in the following discussion of short-term exposure studies are summarized in Table E-1 for both PM_{10} and $PM_{2.5}$ studies.

a. PM_{10} Mortality Studies

The five studies, conducted in ten locations, included in Table IV-2 which reported PM_{10} mortality relationships were examined.

Lower Limit of Detection: This method was applied to the two studies (Birmingham, Schwartz 1993a; Utah Valley, Pope et al., 1992 and Pope and Kalkstein, 1995) which reported concentration-response relationships between mortality and PM_{10} concentrations. Although some nonlinearity may be evident in the nonparametric smoothed curve reported by Schwartz (1993a; 1994g) in the central portion of the range, from approximately 40 - 60 $\mu g/m^3$ (Fig E-1), these are concentrations at which mortality risk is elevated (Samet et al., 1995). Tests failed to indicate the overall PM-mortality relationship could be statistically discriminated from a possible linear relationship (p value of 0.7 for rejecting linearity). The 10th percentile concentration in Birmingham was reported to be 21 $\mu g/m^3$ (Schwartz, 1993a). The nonparametric smoothed curve reported in Pope and Kalkstein's (1995) reanalysis of Utah Valley mortality (Fig. E-2) was also reported as not significantly different from linear ($p>0.5$). In this study, the 10th percentile concentration was not directly reported but is likely to be approximately 20 $\mu g/m^3$, the approximate midpoint of the lowest quintile reported for Utah Valley by Samet et al. (1995). These concentrations are consistent with the lower limit of detection for nonlinearities of 20 $\mu g/m^3$ PM_{10} identified in the CD discussion of PM mortality exposure-response functions (CD, 12-310).

Minimum Mean Concentration: The lowest mean PM_{10} concentration reported in these mortality studies was 30 $\mu g/m^3$, from Schwartz et al. (1996a). This combined mean, averaged across the cities in the study, rather than the lowest mean concentration from any one city in this study, was judged to be appropriate to use for this purpose, since the single monitors used to characterize air quality for each city were sited in locations that may underestimate the average

concentrations experienced across the cities as a whole. The mean concentrations in the three cities in which statistically significant results were reported ranged from 24 - 32 $\mu g/m^3$.

Visual Interpretation: A quintile analysis of a Utah Valley study provided by Pope et al., (1992) suggests that any increased risk associated with the second quintile may be less than the increases associated with the three higher concentration quintiles (Fig. E-3). Alternatively, Samet et al. (1995), using quintiles in a slightly different approach, reported that mortality appeared to increase in the two highest quintiles only (Table E-2). This information would suggest a possible cutpoint of interest in the range of 37 (midpoint of quintile showing reducing increased risk in Fig. E-3) to 42 $\mu g/m^3$ (maximum concentration of quintile showing no increase in risk in Table E-2). The staff judges that the weight given these observations should take into consideration the more recent Utah Valley results discussed above, given the greater sensitivity of the nonparametric methods that have been subsequently been applied to the Utah Valley data.

Various analyses have been done on data from Philadelphia examining PM-mortality relationships using TSP as the measure of PM. Table E-1 also contains converted PM_{10} "cutpoint equivalents" from the TSP findings of these studies that examined TSP concentration-response relationships when associated copollutants were included in the model. There are substantial uncertainties both in interpreting this TSP data in relation to smaller particle indicators (PM_{10}, $PM_{2.5}$) (CD, p. 243), especially when evaluation between copollutants is attempted, and inherent in converting TSP findings into estimates of $PM_{2.5}$. The method and issues involved in deriving these PM_{10} "cutpoint equivalents" are discussed in Section C.

b. PM_{10} Hospital Admissions Studies

Studies conducted in seven locations included in Table IV-2 reporting respiratory and cause-specific hospital admissions relationships with PM_{10} were examined.

Lower Limit of Detection: Nonparametric smooth curves of the concentration-response relationships between PM_{10} and pneumonia (Fig. E-4) and COPD hospital admissions in the elderly in Birmingham have been reported by Schwartz (1994e). No apparent nonlinearities are observed, and the relationships are not statistically distinguishable from linearity ($p \geq 0.25$). The 10th percentile concentration is approximately 19 $\mu g/m^3$. A quartile plot of an analysis of cardiac

hospital admissions for the elderly in Detroit (Schwartz and Morris, 1996) displays increased risk at and above the second quartile (Fig. E-5), with a 25th percentile concentration of 30 $\mu g/m^3$.

Minimum Mean Concentration: The year-long study with the lowest mean PM_{10} concentration, 36 $\mu g/m^3$, reporting significant associations was the Schwartz (1994f) study of COPD and pneumonia hospital admissions among the elderly in Minneapolis. This compares closely to the mean concentration was reported by Thurston et al. (1994) in their study of summertime hospital admissions in Toronto, with a PM_{10} mean concentration of 33 $\mu g/m^3$ averaged across three summers.

Visual Interpretation: The quartile plot of Schwartz (1994d) for elderly pneumonia hospital admissions in Detroit (Fig. E-6) indicates that pneumonia risk may not increase as sharply for the second quartile of PM concentrations as for subsequent quartiles. The midpoint concentration of this second quartile is 37 $\mu g/m^3$.

c. PM_{10} Respiratory Symptoms Studies

The two studies listed in Table VI-2 reporting PM_{10} associations with respiratory symptoms were examined.

Lower Limit of Detection: The Six City study (Schwartz et al., 1994) provides nonparametric smoothed plots for PM_{10} associations with cough (Fig. E-7) and lower respiratory symptoms (Fig. E-8). Statistical tests of deviations from linearity for these associations are not significant. However, the ability to detect nonlinearities is not likely to extend below the 10th percentile concentration of 13 $\mu g/m^3$ PM_{10}.

Minimum Mean Concentration: The Six City study (Schwartz et al., 1994) reports the lower mean PM_{10} concentration of 30 $\mu g/m^3$.

d. $PM_{2.5}$ Mortality Studies

There is less available information concerning $PM_{2.5}$ concentration-response relationships for mortality in comparison to PM_{10}. However, the Harvard Six Cities study (Schwartz et al., 1996a) reports significant associations between $PM_{2.5}$ and mortality in a combined analysis of six cities, as well as associations in individual cities, that indicate that $PM_{2.5}$ mortality associations were relatively consistent in magnitude and statistically significant for three locations (Boston, St. Louis, and Knoxville) with mean concentrations ranging from approximately 16 to 21 $\mu g/m^3$

$PM_{2.5}$ No concentration-response curves were provided, precluding any visual interpretation of results presented in terms of $PM_{2.5}$.

Lower Limit of Detection: For this Six City study, a potential cutpoint could be chosen at the 25th percentile concentration, 9 $\mu g/m^3$, consistent with similar interpretations of studies reporting results in terms of quartile plots.

Minimum Mean Concentration: The $PM_{2.5}$ mean of the combined results from this Six Cities study is 18 $\mu g/m^3$.

Visual Interpretation: Consistent with the approach used above for PM_{10} mortality and discussed more fully in Section C, Table E-1 also gives potential $PM_{2.5}$ "cutpoint equivalents" based on conversions of recent reanalyses of TSP/copollutant concentration-response relationships.

e. $PM_{2.5}$ Hospital Admissions Studies

Minimum Mean Concentration: The only study to examine respiratory hospital admissions directly in terms of $PM_{2.5}$ (Thurston et al., 1994) reported mean concentrations for three summers ranging from approximately 16 to 22 $\mu g/m^3$, with an overall average of approximately 19 $\mu g/m^3$. This is roughly consistent with the more uncertain estimate obtained from the Burnett et al. (1995) study of sulfates and respiratory and cardiac admissions. The mean sulfate concentration of 4.4 $\mu g/m^3$ in that study roughly corresponds to an estimated $PM_{2.5}$ concentration of 15 $\mu g/m^3$.

Lower Limits of Detection: The only study to which this approach can be applied is the Burnett et al. (1995) sulfate study which reports that the respiratory and cardiac hospital admissions from the third quartile were statistically significantly higher than those from the first two quartiles combined. The maximum concentration associated with the bottom two quartiles was approximately 3.0 $\mu g/m^3$ sulfate, the 50th percentile value for the nine Ontario monitoring sites used in the study. To express this finding in terms of a potentially relevant $PM_{2.5}$ cutpoint of interest, a site-specific conversion between SO4 and $PM_{2.5}$ was made using conversion factors for the three largest cities in the study (Toronto, Ottawa, and Windsor), resulting in a $PM_{2.5}$ concentration of roughly 13 $\mu g/m^3$.

f. $PM_{2.5}$ Respiratory Symptoms Studies

Lower Limit of Detection: The Six City respiratory symptoms study (Schwartz et al., 1994) found significant relationships between $PM_{2.5}$ and cough and lower respiratory symptoms in children, although it did not provide either separate quantile or nonparametric smoothed plots for $PM_{2.5}$. Consistent with the approach taken for $PM_{2.5}$ mortality, a potential cutpoint could be chosen at the 25th percentile concentration of 12 $\mu g/m^3$ for this study.

Minimum Mean Concentration: The $PM_{2.5}$ mean concentration for this study (Schwartz et al., 1994) was 18 $\mu g/m^3$.

2. Concentration-Response Relationships Associated with Long-Term PM Exposures

The potential concentration cutpoints identified in the following discussion of short-term exposure studies are summarized in Table E-3 for both PM_{10} and $PM_{2.5}$ mortality studies.

Lower Limit of Detection: The Dockery et al. (1993) Six City study provides plots of long-term mean fine particle concentrations versus adjusted mortality risk for PM_{10} and $PM_{2.5}$. For PM_{10}, increased risks from particles may extend as low as 24 $\mu g/m^3$, the mean concentration for Watertown, which shows an increase in relative risk compared to Portage (Fig. E-9). For $PM_{2.5}$, increased risks may extend as low as 12.5 $\mu g/m^3$, the mean $PM_{2.5}$ concentration for Topeka, which shows a slight increase in relative risk compared to Portage (Fig. E-10).

Minimum Mean Concentration: The mean PM_{10} concentration for the Six City study (Dockery et al., 1993) as a whole was 30 $\mu g/m^3$. The mean $PM_{2.5}$ concentration for the Six Cities study (Dockery et al., 1993) and the mean of the median $PM_{2.5}$ concentrations for each city in the ACS study (Pope et al., 1995) were both reported as 18 $\mu g/m^3$.

Visual Interpretation: For PM_{10}, a case might be made from visually inspecting the results of the Six City study (Dockery et al., 1993) that risk consistently increases only beginning with St. Louis, with a long-term PM_{10} mean of approximately 32 $\mu g/m^3$. For $PM_{2.5}$, a similar case might be made that risk consistently increase beginning with Watertown, with a long-term $PM_{2.5}$ mean of approximately 15 $\mu g/m^3$. Such comparisons, however, are limited by the small number of cities in the study. The ACS study (Pope et al., 1995) provides concentration-response information for $PM_{2.5}$ which appears to more consistently increase at concentrations above the median $PM_{2.5}$ concentration of approximately 15 $\mu g/m^3$ (Fig E-11).

C. Potential Effects of Copollutants or PM Measurement Error on Concentration- Response Relationships

The approach carried out in the sections above for assessing whether underlying nonlinearities exist in PM concentration-response relationships (e.g., resulting from the presence of biological thresholds) uses existing reported concentration-response relationships. The large majority of these relationships were derived considering ambient PM concentrations alone (e.g., without simultaneous inclusion of copollutants). As discussed in Section V.E., several commentors have raised the issue that if the observed concentration-response relationship reflect PM-health effects relationships in which PM is serving as a proxy for other non-considered factors (e.g., the effects of coassociated pollutants, or of total personal exposure to particles) that may causally give rise to health effects, then analyses of observed concentration-response data that do not fully take into account the potential role of these other factors may fail to reveal a genuine underlying nonlinear relationship between ambient PM and health effects. The failure to consider these factors, if they have a genuine causal role, may potentially serve to "disguise" nonlinear concentration-response relationships, and might result in an apparently linear PM concentration-response relationship in cases in which a genuine nonlinear relationship existed.

The two factors advanced as issues of particular concern to consider in this regard have been the influence of coassociated pollutants (Samet et al, 1995; Samet et al., 1996b; Moolgavkar et al., 1995b; Moolgavkar and Luebeck, 1996; Cifuentes and Lave, 1996; Lipfert and Wyzga, 1995b), and the potential influence of different types of measurement error. Measurement error in this context includes concerns over the potential implications that measurements of ambient PM may not accurately reflect total personal exposures to particles, either exposures to all particles or at a mininum a subset of particles including particles of nonambient origin (e.g., from indoor combustion sources). In both the case of potential effects of copollutants and of measurement error, concerns have been raised that available concentration-response relationships may create erroneous estimates of PM-health effects relationships for risk analyses purposes by failing to consider the possibility that these unacknowledged factors may alter the shape of the estimated PM concentration-response relationship.

1. Potential Effects of Copollutants on Determining Effects Thresholds

Several authors have evaluated concentration-response relationships for particles while simultaneously including other combustion source copollutants as variables in the health effects concentration-response regression. Samet et al. (1995) reanalyzed information from Philadelphia for 1973-1980 simultaneously considering SO_2 in the model. One form of presentation they give to their results leads to the question of whether potential TSP effects thresholds exist when copollutants are considered simultaneously. Figure 11 of their report appears to indicate a linear response between mortality and TSP only for TSP > 100 $\mu g/m^3$ (all ages) or TSP > 60 $\mu g/m^3$ (age 65+) (CD, p. 12-311). However, the CD also acknowledges that other approaches undertaken by Samet et al. (1995), such as nonparametric smoothed surfaces simultaneously displaying TSP and SO_2 relationships (CD, pp. 335-344), differs significantly from the simple threshold model shown in their Figure 11 (CD, p. 12-311).

Cifuentes and Lave (1996) analyzed a later period in Philadelphia simultaneously considering two copollutants in the model, SO_2 and O_3. They presented a number of results from several different approaches investigating potential thresholds. The CD finds that Cifuentes and Lave (1996) provides no precise estimate of a change point in the TSP mortality relationship, with the lower portion of a potential cutpoint relationship not showing significance below 60 $\mu g/m^3$ and showing general significance at 90 $\mu g/m^3$ and above (CD, p. 301; Figure 12-32). The study's authors particularly call out the concentration of 78 $\mu g/m^3$ as a concentration below which "the effects of TSP decreased significantly," a concentration representing roughly the midpoint of the range identified by the CD. Although as pointed out by the CD, the methods applied by Cifuentes and Lave do not necessarily imply a slope of zero below the tested cutpoints (CD, pp. 301-302), this central value of 78 $\mu g/m^3$ TSP will be used to summarize the results of their findings in the cutpoint sensitivity analyses for the risk analysis, which does presume a slope of zero below the cutpoint (Appendix F).

To enable the general findings of Samet et al (1995) and Cifuentes and Lave (1996) to be considered in the risk analysis, conversion of their TSP cutpoint findings to fine particles ($PM_{2.5}$) were carried out. Such an approach involves substantial uncertainties both in determining both an appropriate conversion factor to express TSP results as $PM_{2.5}$ as well as the possibility that

substantially different results may have been obtained in the copollutant models if $PM_{2.5}$ data had been available for inclusion in the model rather than the less robust surrogate measure of TSP, especially when discriminations between the particle measure and an associated copollutant are attempted simultaneously in the health model. As indicated by the CD, there is less basis for assuming that analogous results would be obtained for other PM indices, such as PM_{10} or $PM_{2.5}$ (CD, p. 343).

With these concerns in mind, conversion factors were derived from information in Table 6-13 of the CD to allow rough estimates of the potential impacts of application of cutpoints based on the TSP-copollutant analyses of Samet et al. (1995a) and Cifuentes and Lave (1996) to be considered. The Samet et al. (1995) findings were represented by converting the all mortality and elderly 2-D nonparametric smoothed plot findings (reported in Figure 11 of their report) to $PM_{2.5}$ by using the $PM_{2.5}$/TSP ratio (for TSP > 80 $\mu g/m^3$) of 0.36 for the Inhalable Particle Network (IPN), 1979-1983, which provided a rough central estimate $PM_{2.5}$/TSP ratio of 0.36 (CD, Table 6-13). The Cifuentes and Lave (1996) findings were converted to an estimated $PM_{2.5}$ concentration by using the $PM_{2.5}$/TSP ratio available from a site reported to AIRS, 1987-1990 (CD, Table 6-13). Applying these conversions, the Samet et al. (1995) findings could be interpreted as suggesting potential cutpoints in the range of 22 - 36 $\mu g/m^3$ for elderly and all age mortality, respectively, and the Cifuentes and Lave (1996) findings could be interpreted as suggesting the potential for a cutpoint of roughly 29 $\mu g/m^3$ for all age mortality.

Comparable conversions based on Table 6-13 also can be done for PM_{10} , although some additional concern exists for deriving a PM_{10} /TSP conversion factor for Samet et al. (1995) in that the IPN dataset that overlapped the period of study provided information only in terms of PM_{15}. Use of a single monitor operating two years after the study (1982-1983), which was not used in determining the $PM_{2.5}$ conversion factor for Samet et al. (1995) presented previously because the earlier, more extensive network was available, would provide a PM_{10} /TSP conversion factor of approximately 0.57. Use of this factor and a PM_{10} /TSP conversion factor of 0.53 for the AIRS 1987-1991 site provides possible PM_{10} cutpoint concentrations of approximately 34 - 57 $\mu g/m^3$ for the Samet et al. (1995) findings and approximately 43 $\mu g/m^3$ for the Cifuentes and Lave (1996) findings.

For the purposes of sensitivity analyses for the risk analyses, the various cutpoints findings from Samet et al. (1995) and Lave and Cifuentes were represented with a cutpoint of 30 $\mu g/m^3$ $PM_{2.5}$. Given the following considerations: (1) that the Lave and Cifuentes, Samet et al. (1995) findings for the elderly, and the central tendency of the findings for the elderly and all mortality for the two studies combined suggest PM_{10} cutpoints at or below the range of 40 - 45 $\mu g/m^3$, (2) the increased uncertainty in estimating PM_{10} cutpoint equivalents for the Samet et al. (1995) study, and (3) the emphasis of the alternative standards portion of the risk analysis on $PM_{2.5}$, it was judged that there was not a sufficient need to add a separate PM_{10} cutpoint to the sensitivity analyses above 40 $\mu g/m^3$, a concentration that also summarizes the upper end of the analyses of reported concentration-response relationships in Table E-1 (see Summary Section D).

2. Potential Effects of Measurement Error on Determining Effects Thresholds

Another issue to consider in estimating PM concentration-response relationships is the potential effects of measurement error. As discussed in Chapter V, the term measurement error in the broadest sense refers to errors or mis-estimation of several forms that can arise from the use of outdoor monitors to indicate exposure. Measurement error includes both errors resulting from errors in the direct measurement of ambient concentrations, and inaccuracies in the ability of central measurements to proxy for individual exposures, either to ambient pollutant concentrations or potentially the more broad array of particulate pollution from both indoor or outdoor sources to which an individual is personally exposed.

The potential of ambient exposure measurement error (i.e., either error in the direct measurement of ambient concentrations or in the ability of a central monitor to proxy for an individual's exposure to ambient pollutants) to give rise to an apparent more linear-seeming relationship that can disguise an underlying nonlinear relationship has been discussed to some extent in the air pollution and statistics literature (e.g.,Yoshimura, 1990). However, some evidence exists suggesting that the extent of such error may not serve to have large practical significance for current ambient particle concentration-response relationships. As discussed in Section V.E., Schwartz et al. (1996a) reported that statistical relationships between ambient $PM_{2.5}$ concentrations and mortality were observed even when the analysis was restricted to

only days with $PM_{2.5}$ concentrations of 25 μg/m^3 or below. A number of other studies (Pope, 1991; Schwartz et al.,1993a; Schwartz, 1994d; Schwartz, 1994e; Schwartz, 1994f) have excluded higher PM concentrations (e.g., PM_{10} concentrations above 150 μg/m^3). The similar or slightly larger relative risks observed in these studies when days with high concentrations are excluded from the analysis suggests that it is unlikely that measurement error is serving to disguise a nonlinear relationship that extends far into the range of observed concentrations. These studies also suggest that any "personal exposure measurement error" (errors in the ability of a central monitor to proxy for an individual's total exposure to indoor and outdoor particles, or some relevant subset of total exposure such as, exposures to all outdoor and indoor combustion sources), if present, may be affecting reported ambient $PM_{2.5}$ concentration-response relationships to only a limited extent. If ambient particle exposures are associated with mortality risk at 25 μg/m^3 $PM_{2.5}$ or below, it seems unlikely that a nonlinear concentration-response relationship with little or no risk for ambient particles may be being "disguised" by the unacknowledged role of other particle exposures, since relationships between ambient $PM_{2.5}$ and health effects, in general, would not be expected to be influenced by exposures to nonambient indoor sources, which are largely independent of ambient exposures (CD, p.1-10).

To allow for assessment of the potential effects on the risk analysis if measurement errors were found to be substantially affecting the shape of reported concentration-response relationships, cutpoint concentrations and slope adjustments of the type described in Chapter VI can be used to remodel ambient concentration-relationships to reflect hypothetical measurement error. For this purpose, although they were originally derived using the results from other lines of investigation, the cutpoint levels effects selected in Section D of this Appendix, which provide cutpoints across a substantial portion of the lower range of ambient concentrations, can be used to also model the possibility that measurement errors might be obscuring a nonlinear ambient concentration response function with little or no risk in this lower range of concentrations. For example, the possibility that exposure error might be obscuring ambient concentration-response nonlinearities at cutpoints of 10, 18 and 30 μg/m^3 $PM_{2.5}$ can be examined. Although the very issue raised by concerns about measurement error

is that these reported functions may "disguise" nonlinearity through the operation of errors in measurement of exposure, the results of the analyses in Sections A - C.1 above generated generate a set of potential cutpoints that include substantial PM concentrations, and thus for practical purposes can be used to examine of the potential impacts of substantial measurement error as well.

D. Summary

Staff believes that it is most appropriate to combine the potential concentration cutpoints summarized in Tables E-1 and E-3 into a few cutpoints for the purpose of doing sensitivity analyses. Combining information across studies, effects, and alternative approaches avoids giving undue weight to any particular study or approach. From these efforts, the following specific cutpoints judged of use for illustrating the sensitivity of risk analyses results have been identified:

- Short-term PM_{10} studies: 20, 30, 40 $\mu g/m^3$
- Short-term $PM_{2.5}$ studies: 10, 18, 30 $\mu g/m^3$
- Long-term PM_{10} studies: 24, 30, 32 $\mu g/m^3$
- Long-term $PM_{2.5}$ studies: 12.5, 15, 18 $\mu g/m^3$

These cutpoints were derived for the purposes of obtaining a reasonable range of possible cutpoints for the purposes of investigating the potential sensitivity of the risk analyses results to alternative concentration-response relationships reflecting alternative interpretations of reported relationships, potential changes in the concentration-response relationships from the consideration of copollutants, and/or potential effects of different types of measurement error. The material in Appendix E is not intended to be a critical or rigorous assessment of relative weight of evidence for any particular cutpoints from the available literature.